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SPECIAL ARTICLE

Society of Critical Care Medicine Guidelines for the Administration of Neuromuscular Blockade in Adults With Acute Respiratory Distress Syndrome

RATIONALE: Neuromuscular blocking agents (NMBAs) show potential benefits on mortality and other complications of acute respiratory distress syndrome (ARDS) in adult patients. Evidence-based decisions and processes ensure appropriate use of neuromuscular blockade in adult patients with ARDS.

OBJECTIVES: The objective of these guidelines was to develop evidence-based recommendations for the administration of NMBAs in critically ill adult patients with ARDS.

DESIGN: The American College of Critical Care Medicine Board convened a 21-member multidisciplinary panel of experts in critical care medicine, nursing, respiratory therapy, pharmacology, surgery, neurology, and anesthesiology. The panel included two expert methodologists specialized in developing evidence-based recommendations in alignment with the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) methodology. Conflict-of-interest policies were strictly followed during all phases of guidelines development including task force selection and voting.

METHODS: The panel members identified and formulated five Population, Intervention, Comparison, and Outcome questions. We conducted a systematic review for each question to identify the best available evidence, statistically analyzed the evidence, and assessed the certainty of the evidence using the GRADE methodology. We used the GRADE evidence-to-decision framework to formulate the recommendations.

RESULTS: The panel generated two conditional recommendations. One recommendation is to use NMBAs in adults with ARDS with Pao_2/Fio_2 less than 150. For the other recommendations, there was equipoise in the recommendation for and against using titratable vs. fixed-dose NMBA dosing, a monitoring-based strategy for assessing depth of sedation and analgesia in adults with ARDS before initiating or while receiving neuromuscular blockade, and administration of NMBAs for patients who are proned, due to overall lack of evidence in critically ill patients and due to considerations of patient safety and experience concerns.

CONCLUSIONS: These guidelines provide additional perspectives on the use of NMBA in patients with ARDS, recognizing that institutional and patient-specific considerations must help to guide the decision-making process.

KEYWORDS: acute respiratory distress syndrome; critical care; critical illness; intensive care unit; neuromuscular blocking agents; practice guidelines

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These guidelines on neuromuscular blocking agents (NMBAs) in critically ill patients are the fourth of a series, with prior versions published in 1995, 2002, and 2016 (1–3). Previously addressed topics include indications, selection of specific NMBAs, and mitigation of adverse events. This update was prioritized to address evolving sedation strategies, new data on NMBA use for the acute respiratory distress syndrome (ARDS) and rising use of prone positioning. The current guidelines address five high-yield Population, Intervention, Comparator, and Outcome (PICO) questions in accordance with the revised Society of Critical Care Medicine (SCCM) development process, with a focus on ARDS, as this high-mortality condition is the most common indication for the sustained administration of NMBA in critically ill patients (4).

METHODOLOGY

The American College of Critical Care Medicine, the consultative body of SCCM, commissioned an international multidisciplinary panel of experts in critical care medicine; it included a diverse group of physicians, nurses, pharmacists, respiratory therapists, and methodologists. Members of the panel were required to disclose conflicts of interest per the SCCM policy, which were reassessed at each phase of the guidelines process.

The panel created five consensus-based PICO questions about clinically relevant topics related to NMBA use in ARDS. The core question of using NMBAs in ARDS was chosen in addition to topics not addressed by prior versions of the guidelines (**Table S1**, https://links.lww.com/CCM/H864). The panel then selected patient-oriented, clinically relevant outcomes and rated their relative importance (**Table S2**, https://links.lww.com/CCM/H864). A systematic review was then performed, including articles published through June 2024. The search was conducted by a medical librarian using MEDLINE, Embase, CENTRAL, ClinicalTrials.gov, and World Health Organization International Clinical Trials Registry Platform; search strategies are provided in the **Supplemental Materials** (https://links.lww.com/CCM/H864). Search results were uploaded to Covidence (Veritas Health Innovation, Melbourne, VIC, Australia) (5) for screening, full text review, and data extraction.

Data extraction and risk of bias assessment was performed independently and in duplicate by two experienced methodologists using pre-piloted forms. Where there were disagreements, they were resolved by discussion between methodologists until consensus was reached. The risk of bias assessment was performed by the methodologist. The risk of bias for randomized controlled trials (RCTs) was assessed using the Cochrane Risk of Bias tool 1 for RCTs (6).

Meta-analyses were performed on the outcomes of interest (**Figs. S1–S18**, https://links.lww.com/CCM/H864) for each PICO question using RevMan, Version 5.4 (The Cochrane Collaboration, London, United Kingdom) (7). Data that could not be quantitatively pooled or outcomes with insufficient studies to analyze were addressed narratively.

Recommendations were then developed using the Grading of Recommendations, Assessment, Development, and Evaluation process (8). The evidence-to-decision (EtD) framework was completed by the panel using GradePro software (Evidence Prime, Hamilton, ON, Canada) (9) for each PICO to develop a draft recommendation that considered the balance of desirable and undesirable effects, certainty of evidence, resource considerations, feasibility, acceptability, and equity considerations; EtD worksheets can be found in the Supplemental Materials (https://links.lww.com/CCM/H864). Recommendations had to receive at least 80% of the vote of the panel to be approved. These clinical practice guidelines reflect the state of knowledge at the time of publication.

RECOMMENDATIONS

The recommendations in these guidelines are summarized in **Table 1**. They define principles of practice applicable in most situations but may not meet the needs of patients in all jurisdictions (e.g., low- and middle-income countries). Each recommendation was designated either "Strong" or "Conditional" (**Table 2**), and the rationale for each recommendation is presented below.

Neuromuscular Blockade vs. No Neuromuscular Blockade

PICO 1: Among adult patients with ARDS, should neuromuscular blockade vs. no neuromuscular blockade be administered to improve outcomes?

Recommendation 1: We suggest using NMBAs over not using NMBAs in adults with ARDS with Pao_2/Fio_2 less than 150 who are persistently hypoxemic

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TABLE 1.
Recommendations

No.	Recommendation	Strength	Certainty of Evidence
1	We suggest using NMBAs over not using NMBAs in adults with ARDS with $Pao_2/Fio_2 < 150$ who are persistently hypoxemic and/or not achieving mechanical ventilation targets on sedation	Conditional for	Low
2	We suggest using either a fixed-dose strategy without monitoring depth of neuromuscular blockade, or a titration-based strategy by monitoring depth of neuromuscular blockade for adults with ARDS	Conditional for	Very low
3	We suggest using either a scale-based evaluation or nonscale-based evaluation for depth of analgesia and sedation before initiating NMBA for adult patients with ARDS	Conditional for	Very low
4	We suggest using either a monitoring-based strategy or no monitoring of depth of analgesia and sedation in adults with ARDS who are receiving NMBAs	Conditional for	Very low
5	We suggest either administering neuromuscular blockade or not administering neuromuscular blockade in adult patients who are proned for ARDS	Conditional for	Very low

ARDS = acute respiratory distress syndrome, NMBAs = neuromuscular blocking agents.

TABLE 2.
Strength of Recommendation

Stakeholders	Strong Recommendation	Conditional Recommendation
Patients	Nearly all individuals in a given situation would want the recommended intervention; only a small proportion would not	The majority of individuals in a given situation would want the suggested recommendation, but a significant minority would not
Clinicians	Nearly all patients should receive the recommended intervention. Adherence to this recommendation could potentially be used as a quality indicator	Different choices will be appropriate for different patients, and clinicians should expect to spend more time on decision-making, taking into account a patient's specific circumstances, preferences and values. Policy-making will require substantial debate and input from many stakeholders

and/or not achieving mechanical ventilation targets on sedation (conditional recommendation for, low certainty of evidence).

Remarks: We emphasize ventilator and/or sedation optimization to achieve lung-protective ventilation, mitigate dyssynchrony, and improve oxygenation before considering neuromuscular blockade. If used, neuromuscular blockade should be limited in duration and not routinely exceed 48 hours.

Rationale

Twenty-Eight-Day Mortality. A meta-analysis of seven RCTs (10–16) including 1598 patients demonstrated a decreased risk of 28-day mortality with NMBA compared with controls relative risk (RR, 0.74; 95% CI, 0.56–0.98). The certainty of evidence was downgraded to low for high risk of bias and inconsistency due to heterogeneity across trials. A meta-analysis of three RCTs (10, 11, 15) including 428 patients subgrouped by severity of hypoxemia of Pao_2/Fio_2 less than 150 demonstrated a decreased risk of 28-day mortality, RR of 0.70 (95% CI, 0.55–0.90), with NMBA compared with control (10). Forest plots on 28-day mortality are presented in Figures S1 and S2 (https://links.lww.com/CCM/H864).

ICU Mortality. A meta-analysis of four RCTs (10–12, 15) including 455 patients (Fig. S3, https://links.lww.com/CCM/H864) demonstrated a decreased risk of ICU mortality with NMBA compared with controls (RR, 0.73; 95% CI, 0.58–0.93). The certainty of the

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evidence was downgraded to moderate due to imprecision associated with small sample size.

In-Hospital Mortality. A meta-analysis of five RCTs (10, 11, 14–16) including 1478 patients demonstrated a decreased risk of in-hospital mortality with NMBA compared with controls (RR, 0.78; 95% CI, 0.60–1.01). A meta-analysis of four RCTs (10, 11, 14, 15) including 1437 patients subgrouped by severity of hypoxemia (i.e., $Pao_2/Fio_2 > 100$ and $Pao_2/Fio_2 \leq 100$) demonstrated a decreased risk of in-hospital mortality with NMBA compared with controls (RR, 0.87; 95% CI, 0.71–1.06 and RR, 0.95; 95% CI, 0.82–1.11, respectively). Forest plots are presented in Figures S4 and S5 (https://links.lww.com/CCM/H864). The certainty of the evidence was downgraded to low for inconsistency due to significant heterogeneity across the trials and imprecision.

Ninety-Day Mortality. The ARDS et Curarisation Systematique (ACURASYS) trial by Papazian et al (15) 2010 demonstrated a significant reduction in 90-day mortality in patients receiving a 48-hour continuous infusion of cisatracurium in combination with deep sedation (Ramsay Sedation Score 6) compared with those receiving deep sedation alone. The Prevention and Early Treatment of Acute Lung Injury-Reevaluation of Systemic Early Neuromuscular Blockade (PETAL-ROSE) trial by Moss et al (14) 2019 comparing the use of cisatracurium to light sedation (Richmond Agitation-Sedation score 0 to –1) found no significant difference in 90-day mortality between the strategies. Of note, high-dose infusions of cisatracurium were employed in both trials. Potential explanations for the differences between these two major RCTs (14, 15) include lack of blinding and use of lighter sedation in the control group for PETAL-ROSE. There was also decreased use of prone positioning and a ventilator strategy of higher positive end-expiratory pressure in PETAL-ROSE, possibly leading to decreased atelectasis in these patients. These findings suggest that continuous infusions of NMBAs should be reserved for patients with moderate-to-severe ARDS already receiving deep sedation, which is likely consistent with clinical practice, as a recent survey of U.S. intensivists found that 85.5% of respondents stated that they used NMBA infusions only after a trial of deep sedation (17).

ICU Length of Stay. An analysis of one RCT (15) subgrouped by length of stay in all randomized patients (n = 339) and survivors (n = 224) demonstrated a mean decrease of –1.80 days (95% CI, –5.93 to 2.33 d) and –2.90 days (95% CI, –7.86 to 2.06 d), respectively, with NMBA compared with controls (Fig. S6, https://links.lww.com/CCM/H864). The certainty of the evidence was downgraded to low due to imprecision (small sample size and wide CIs).

Ventilator-Free Days. A meta-analysis of six RCTs (10–12, 14–16) including 1502 patients demonstrated a mean increase in ventilator-free days of 0.57 (95% CI, –0.43 to 1.57) with NMBA compared with controls (Fig. S7, https://links.lww.com/CCM/H864). The certainty of evidence was downgraded to moderate for imprecision.

Mechanical Ventilation Days. A meta-analysis of three RCTs (10, 11, 15) including 431 patients demonstrated a mean decrease in duration of mechanical ventilation in all randomized patients of –1.21 days (95% CI, –4.23 to 1.81 d) with NMBA vs. controls. A subgroup analysis of survivors in these trials (n = 268) demonstrated a mean increase in duration of mechanical ventilation of 0.25 days (95% CI, –5.48 to 5.99 d) with NMBA compared with controls. A forest plot is presented in Figure S8 (https://links.lww.com/CCM/H864). The certainty of evidence was downgraded to very low for inconsistency due to significant heterogeneity across the trials and imprecision.

Adverse Events. Meta-analyses of four RCTs (10, 11, 14, 15) including 1437 patients demonstrated decreased risk of barotrauma (RR, 0.55; 95% CI, 0.35–0.85), increased risk of ICU-acquired weakness (RR, 1.16; 95% CI, 0.98–1.37), and increased risk of total adverse events (RR, 1.63; 95% CI, 0.98–2.72), with NMBA compared with controls. Adverse events included pneumothorax, ventilator-associated pneumonia, neuromyopathy, septic shock, ICU-acquired paresis, bradycardia, barotrauma, ileus, paralysis awareness, hyperkalemia, myopathy, methemoglobinemia, and a variety of cardiac, respiratory, and nervous system events. Forest plots are presented in Figures S9–S11 (https://links.lww.com/CCM/H864).

Additional Considerations. The overall certainty of evidence on use of NMBA in ARDS was low (**Table S3**, https://links.lww.com/CCM/H864). The panel chose this question despite being addressed by other guidelines given the foundational nature of addressing this question in an evidence-based framework before focusing on follow-up PICO questions. The panel discussed associated considerations, including dosing (intermittent vs. bolus), agent selection, and duration of use and concluded that further research is needed before making formal recommendations on these details. The panel judged the costs associated with the use of

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NMBAs to be moderate, albeit with geographic variation. These include both the direct cost of NMBAs and co-administered drugs (e.g., sedatives), as well as indirect costs such as length of stay and need for rehabilitation due to weakness. They also considered that there may be variability in patient preferences on the importance of outcomes such as ICU-acquired weakness, which is an issue that must be addressed with further research. The panel was uncertain regarding the impact on health equity. The panel judged that the use of NMBAs is feasible and probably acceptable to key stakeholders despite costs and known adverse events (see EtD worksheet; **Table S4**, https://links.lww.com/CCM/H864).

Titration of Neuromuscular Blocking Agents vs. Fixed-Dose Strategy

PICO 2: Among adult patients with ARDS who receive neuromuscular blockade, does titrating NMBAs by monitoring depth of neuromuscular blockade vs. using a fixed-dose strategy without monitoring depth of neuromuscular blockade improve patient outcomes?

Recommendation 2: We suggest using either a fixed-dose strategy without monitoring depth of neuromuscular blockade, or a titration-based strategy by monitoring depth of neuromuscular blockade for adults with ARDS (conditional recommendation for, very low certainty of evidence).

Remarks: Given the limitations of existing evidence, clinical decision-making regarding titration-based or fixed-dose strategies should be tailored to individual patient characteristics and needs.

Rationale

No RCTs were found that directly addressed this question. The limited data that does exist compares a fixed-dose strategy to dosing based on titration to train-of-four (TOF) testing, with no clear differences in outcomes (18, 19). Using a fixed-dose strategy without monitoring depth of blockade comes with the risk of either insufficient or excessive diaphragm paralysis. Additionally, compared with peripheral muscles, the diaphragm is more resistant to neuromuscular blockade, and its activity may correlate differently to TOF ratios (20). Guidelines for NMBA use in the operative setting specifically call for quantitative neuromuscular monitoring whenever NMBAs are given, throughout all phases of anesthesia from before initiation of neuromuscular blockade until recovery of the TOF ratio to greater than 0.9 (21). Despite these practices being established outside critical care, further research is needed to understand the implications for either strategy in critically ill patients with ARDS. Regardless of the strategy used, clinicians are encouraged to assess for depth of blockade as well as possibility of residual blockade after cessation of NMBAs.

Sedation Evaluation Using Scale-Based vs. Nonscale-Based Strategies Before NMBA Initiation

PICO 3: Before initiation of neuromuscular blockade in adult patients with ARDS, does the use of a scale-based strategy vs. a nonscale-based clinical evaluation of depth of analgesia and sedation improve outcomes?

Recommendation 3: We suggest using either a scale-based evaluation or nonscale-based evaluation for depth of analgesia and sedation before initiating NMBA for adult patients with ARDS (conditional recommendation for, very low certainty of evidence).

Remarks: Given the limitations of the evidence, patient characteristics, availability of monitoring tools, clinician and institutional expertise with available tools, and costs (direct and indirect) should all be considered when selecting a monitoring-based strategy beyond usual clinical assessments. Regardless of strategy chosen, clinicians should ensure adequate depth of sedation before initiating NMBAs, with the goal of maintaining patient safety and reducing distress, despite lack of evidence.

Rationale

Scale-based strategies use standardized scoring systems to assess the level of sedation or pain relief to try to ensure consistency and objectivity in assessments. Examples of clinical scales include the Richmond Agitation-Sedation Scale for sedation or the Critical Care Pain Observation Tool for pain (22). Other quantitative methods for monitoring the depth of sedation include monitoring devices such as electroencephalography and bispectral index (BIS) (23). Nonscale-based clinical evaluation relies on clinician judgment, experience, and observational skills to assess the level of sedation or analgesia by using vital signs (tachycardia, hypertension, diaphoresis) and assessing body

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movements and/or patient-ventilator interactions. There was no systematic evidence comparing different monitoring strategies for sedation and analgesia despite emphasis in several NMBA-related guidelines on reducing unintended patient awareness and recall (24–28). The EtD worksheet is presented in **Table S5** (https://links.lww.com/CCM/H864).

Monitoring Depth of Analgesia/Sedation vs. No Monitoring While Receiving NMBA

PICO 4: While receiving NMBAs in adult patients with ARDS, is there a role for monitoring depth of analgesia and sedation vs. not monitoring depth of analgesia and sedation to improve patient outcomes?

Recommendation 4: We suggest using either a monitoring-based strategy or no monitoring of depth of analgesia and sedation in adults with ARDS who are receiving NMBAs (conditional recommendation for, very low certainty of evidence).

Remarks: Given the evidence limitations, clinicians should consider patient characteristics, availability of and local expertise with monitoring tools for evaluating depth of sedation and analgesia, and associated costs (direct and indirect) when deciding whether to implement a monitoring-based strategy beyond usual clinical assessments. Adequate depth of analgesia and sedation during administration of NMBAs should be ensured, with the goal of maintaining patient safety and minimizing distress, despite lack of evidence.

Rationale

Pain monitoring strategies that have been used in critically ill patients who are pharmacologically paralyzed include heart rate variability-based Analgesia Nociception Index (29), video pupillometry-based pupillary pain index (30), but larger scale validation and cost-benefit analyses are needed. Similarly, accurate, validated tools are needed for quantitative monitoring of sedation. Special equipment and expertise are needed for electroencephalogram-based evaluation, limiting its scalability in critical care. BIS monitors, commonly used in the operative setting, may be inaccurate in discerning levels of sedation. In one study by Schuller et al (31) 2015, two of ten fully awake volunteer participants receiving neuromuscular blockade had BIS values consistent with deep sedation.

Analyses of relevant studies demonstrated no significant difference in analgesia rate adjustment (32), delirium/coma-free days (32), ICU-free days (32), ICU length of stay (33, 34), duration of mechanical ventilation (34), 90-day mortality (32–34), self-extubation (32), and ventilator-free days (32, 33) with monitoring depth of sedation compared with no monitoring in patients with ARDS who were receiving NMBA. Forest plots of these analyses are presented in Figures S12–S18 (https://links.lww.com/CCM/H864).

The overall quality of evidence was very low due to risk of bias associated with study design, and imprecision attributed to small sample size and wide CIs for either analgesia or sedation monitoring (**Table S6**, https://links.lww.com/CCM/H864). The balance of benefits and harms did not favor either a monitoring-based strategy or a nonmonitoring-based strategy, as more sedation and analgesia adjustments may have both positive and negative implications.

The panel was uncertain regarding the resources required to implement monitoring-based strategies and its impact on healthcare equity given the widespread variation in the availability of monitoring devices, even if validated. The panel judged that the acceptability of a monitoring-based strategy to key stakeholders would vary but is probably feasible to implement in clinical practice (EtD worksheet; **Table S7**, https://links.lww.com/CCM/H864). Until better evidence is available in critical care settings, clinicians may consider modalities employed in noncritical care settings (e.g., intraoperative neuromuscular blockade) using ICU specific clinical checklists or protocols developed based on institutional expertise and availability of monitoring strategies. Clinicians should evaluate depth of analgesia and sedation during opportunities that involve NMBA interruption.

Patients Who Are Proned for ARDS

PICO 5: Among adult patients who are proned for ARDS, does administration of neuromuscular blockade vs. no neuromuscular blockade improve outcomes?

Recommendation 5: We suggest either administering neuromuscular blockade or not administering neuromuscular blockade in adult patients who are proned for ARDS (conditional recommendation for, very low certainty of evidence).

Remarks: Given the limited evidence, consider patient factors and local proning practices should be

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TABLE 3.
Research Priorities

Topic	Research Priorities
Neuromuscular blockade administration	Optimal trigger for initiating NMBA (e.g., relative to course early vs. late, relative to depth of sedation, cutoff based on Pao_2/Fio_2 ratios, relative to the presence of pulmonary mechanics or relative to the presence of right ventricular dysfunction, or use of multimodality scores like Murray score)
	Efficacy of different NMBAs
	Interplay between different modes of mechanical ventilation and use of NMBAs
	Reproducibility of results evaluating NMBAs in ARDS across different global population subsets (high- vs. low-resource critical care settings, interplay between patent-related factors, age, gender, ethnicity, and ARDS et Curarisation Systematique/Prevention and Early Treatment of Acute Lung Injury-Reevaluation of Systemic Early Neuromuscular Blockade (ACURARYS)/Prevention and Early Treatment of Acute Lung Injury-Reevaluation of Systemic Early Neuromuscular Blockade (PETAL-ROSE) restricted to France and the United States)
	Healthcare utilization metrics vs. patient-reported clinical outcomes with regard to analgesia and sedation practices (less ICU-acquired weakness may be meaningful for the patient compared with two extra days of hospitalization)
Titration/dosing of NMBAs	Mechanism of benefit of NMBAs (could impact dosing strategy)
	Influence of dosing strategy–complete vs. deep block on adverse events and outcomes
	Target for depth of blockade when using quantitative monitoring (ventilator synchrony, TOF)
	Optimal metrics on peripheral nerve stimulation monitoring–TOF ratio, TOF count, post-tetanic count, frequency, goals, quality of monitoring, etc
	Dose with vs. without steroids, need to change dose for prolonged durations
	The benefit of NMBA may be a function of ARDS phenotype in patients with increased respiratory system elastance, an area for future research
	Patient-centered NMBA dosing based on the effect of NMBA blockade based on age, sex, pregnancy, coexisting renal or hepatic disease and by coexisting drugs like calcium channel blockers, antiarrhythmic agents, steroids, electrolyte imbalance, and aminoglycoside antibiotics
Scale-based strategies for clinical evaluation of depth of analgesia and sedation	Differences in the specific drugs used for analgesia and sedation
	Drug dosing strategies, use of single vs. combination drugs for analgesia and sedation
	Analgesia and sedation monitoring strategy for goals before blockade
Monitoring depth of analgesia/sedation	Differences in the specific drugs used for analgesia and sedation
	Drug dosing strategies, use of single vs. combination drugs for analgesia and sedation
	Analgesia and sedation monitoring strategy for goals before blockade
	Comparing the efficacy and accuracy of different monitoring tools, recognizing that monitoring raises different issues in the ICU vs. operating room
	Healthcare utilization metrics vs. patient-reported clinical outcomes with regard to analgesia and sedation practices
	Evaluation of specific outcomes deemed important for but not evaluated in the current literature (e.g., quality of life, cognitive function, psychologic outcomes)
Patients who are proned for ARDS	NMBA first or prone first?
	If already paralyzed and now considering proning–when to prone patients, which patients to prone, and how long to prone
	Factors influencing outcomes (e.g., level of sedation and use of prone positioning)

ARDS = acute respiratory distress syndrome, NMBAs = neuromuscular blocking agents, TOF = train-of-four.

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factored into clinical decision-making about NMBA use during prone positioning.

Rationale

In the Prone Positioning in Severe ARDS Patients (PROSEVA) RCT (35), which assessed the impact of early use of prone positioning on patient outcomes, the concurrent use of NMBAs was common, used in 91% of proned patients, and 82.3% of those in the control arm. While the PROSEVA trial demonstrated a mortality benefit with prone positioning, it did not provide insight into the potential synergistic or antagonistic effect of NMBA in the prone position. Observational data from patients with COVID-19-related ARDS suggests that NMBA administration in proned patients improves oxygenation, although there is no evidence that this translated to improved patient-centered outcomes (36). In a survey of 342 ICU physicians in a U.S.-based subset of 12 ICUs (75% medical), 34% responded that an NMBA should be reserved until after proning, suggesting that there is variability in clinical practice (17). Further research is needed to determine if the use of NMBAs improves outcomes in this population.

RESEARCH AGENDA

The panel raised several issues for future research. Clear criteria for initiating neuromuscular blockade—such as Pao_2/Fio_2 ratios, failure to achieve lung-protective ventilation, or resolve ventilator dyssynchrony—have not been systematically addressed. While most clinical trials have used Pao_2/Fio_2 less than 150 as an inclusion criterion, further research is needed to define these thresholds more precisely. Although fixed, high-dose, 48-hour cisatracurium infusions were used in previous trials, it is unclear if this dosing, duration, or NMBA agent is necessary or appropriate for all patients (14, 15). We need mechanistic hypothesis-driven research on best monitoring paradigms for neuromuscular blockade. Is the depth of blockade enough if it addresses ventilator dyssynchrony without achieving peripheral neuromuscular blockade? What are the best strategies for optimal sedation and analgesia before and during NMBA use? (14, 15) NMBAs are also often used in combination with other supportive measures for ARDS, such as prone positioning, high positive end-expiratory pressure, and corticosteroids. Additional data are needed to understand whether the addition of NMBAs to these therapies is synergistic or antagonistic. These are all questions for future research. A summary of research priorities is presented in **Table 3**.

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